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10/696,572	10/30/2003	Masataka Andoh	016778-0470	5923
22428 7590 08/03/2009 FOLEY AND LARDNER LLP SUITE 500 3000 K STREET NW WASHINGTON, DC 20007				
EXAMINER DEJONG, ERIC S				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/696,572

**Applicant(s)**

ANDOH ET AL.

**Examiner**

ERIC S. DEJONG

**Art Unit**

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 April 2009.  
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-5, 7-17, 19-25 and 27-34 is/are pending in the application.  
4a) Of the above claim(s) 4, 16, 29, 30 and 32-34 is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 1-3, 7-15, 17, 19-25, 27, 28 and 31 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_  
5) ☐ Notice of Informal Patent Application  
6) ☐ Other: \_\_\_\_\_

## **DETAILED OFFICE ACTION**

Applicants response filed 04/02/2009 is acknowledged.

Claims 6, 18 and 26 are cancelled. Claims 1-5, 7-17, 19-25, and 27-34 are pending. Claims 4, 16, 29, 30, and 32-34 are withdrawn as being drawn to a non-elected species (see applicants response filed 05/16/2006 and page 2 of the Office action mailed 09/15/2006). Claims 1-3, 5, 7-15, 17, 19-25, 27, 28, and 31 are currently under examination.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 5, 7-15, 17, 19-25, 27, 28, and 31 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The following rejection is newly applied.

The recent en banc decision regarding *Bilski v. Warsaw* (2008) set forth that a process is patent-eligible if (1) it is tied to a particular machine or apparatus or (2) it

transforms a particular article into a different state or thing. Further, the recent decision in *Comiskey* (2009) confirmed the opinion set forth in *Bilski* of the prohibition pre-empting an abstract idea or mental process in a claim. The revised *Comiskey* decision further reiterated the precedent set forth in *Richman*, 563 F.2d 1026, 1030 (CCPA 1977) wherein the court held the application unpatentable because "if a claim [as a whole] is directed essentially to a method of calculating, using a mathematical formula, even if the solution is for a specific purpose, the claimed method is nonstatutory."

The instant claims are drawn to a method and related computer apparatus and program for the correction of microarray data. The claimed process, which is further carried out by said computer related apparatus and program, involves the abstract and computational steps of inputting gene expression intensity data, standardizing said gene expression intensity data, outputting said standardizing gene expression intensity data, estimating distortion, outputting a first corrected gene expression intensity data, performing an S-D transformation of said data, and outputting a second corrected gene intensity data. The instant claims do not recite or inherently involve any transformation of a particular article, therefore the Examiner must determine if the instant claims have a tie to a particular machine or apparatus. Instant claims 13-15, 17, 19-25, and 31 do not recite any limitation directed to a particular apparatus. The recitation of an output to a display in said claims has been treated as insignificant post solution activity as the display is not involved in the steps directed toward the correction of microarray data. Further, both the apparatus and computer readable embodiments as set forth in claims 1-3, 5, 7-12, 27, and 28 serve only as general purpose computing means that perform

the method as set forth above, and as such wholly preempt an abstract process. Therefore, the instant claims are directed towards non-statutory subject matter.

### ***Response to Arguments***

Applicant's arguments filed 04/02/2009 have been fully considered but they are not persuasive.

In regards to the rejection of claims under 35 USC 101 as being directed to non-statutory subject matter, applicants argue that the instant claims are directed to a "system" and have been amended to recite a data analyzer processor that standardizes data and a data analyzer processor. In the instant case, the claims recite a "data standardization unit, a spot-based correction unit, and a sum difference plot based correction unit, all of which are "configured" to perform an abstract series of computational and abstract steps as set forth in claim 1. The "system" as instantly claimed presents nothing more than a general purpose computer comprising unspecified programming that carries out said series of computational and abstract steps. The only utility for such a "system" is the abstract computational operations that it may carry out, and as such would wholly pre-empt said abstract computational process. Therefore, the examiner maintains that the instant claims are directed towards non-statutory subject matter.

***Claim Rejections - 35 USC § 112, Second Paragraph***

The rejection of claims 1-3, 5, and 7-12 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of amendments made to the instant claims.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 13-14, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang et al. (Nucleic Acids Research, 2002, Vol. 30, pages 1-10) in view of Weng (US PGPUB 2003/0226098).

Claim 1 is drawn a cDNA microarray data correction system for correcting global an local distortions of microarray data and correcting measurement errors caused by a difference in sensitivity between fluorescent dyes comprising five steps.

The preamble of claim 1 is taught in the first two sentences of the abstract of Yang et al. which states:

There are many sources of systematic variation in cDNA microarray experiments which affect the measured gene expression levels (e.g. differences in labeling efficiency between the two fluorescent dyes). The term normalization refers to the process of removing such variation.

The first step of the body of instant claim 1 states gene expression intensity data is input and background noise is removed. The passage under "Image processing" in column 2 of page 2 of Yang et al. states:

Each hybridization produced a pair of 16-bit images, which were processed using the software package Spot. The main quantities of interest produced by the image analysis methods (segmentation and background correction) are the (R,G) fluorescence intensity pairs for each gene on each array (where R = red for Cy5 and G = green for Cy3). Note that we call the spotted DNA sequences 'genes,' whether they correspond to actual genes, ESTs or DNA sequences from other sources.

The second step of data standardization using grid-by-grid order statistics for inputting and transmitting gene expression data is described at the top of page 3, column 1 of Yang et al., which is entitled, "Within-print tip group normalization" and is based in part on grid data. The model listed is used to input and transmit data.

The third step of instant claim 1 is a first correction means for performing a distortion depending on a spot position on grid coordinates for the standardized gene expression intensity data. The "Scale normalization" section in column 1 (line 8) of page 3 of Yang et al. teaches such a normalization. The equations in this section illustrate a nonparametric smoothing method.

The fourth step of instant claim 1 is a second correction means for performing a distortion depending on a spot position on grid coordinates for the standardized gene expression intensity data. The "Composite normalization" section in column 1 (line 8) of

page 3 of Yang et al. teaches such a second correction means. In addition, the "Intensity-dependent normalization" at the bottom 10 lines of column 2 of page 2 of Yang et al. describes the use of MA plots (i.e. output) and could also serve as a second correction means for the data.

The instant claims have further been amended to recite "wherein the standardized gene expression intensity data is represented by a sum of a true gene intensity and distortion depending on the spot. While not expressly taught by Yang et al., the resultant gene expression intensity data as recited in the instant claim reads only on a reorganization of data, per se, and does not serve to produce any new or useful information beyond that which was already present and apparent to one having ordinary skill in the art. As such, the reorganization of data as instantly claimed fails to differentiate the instant claims from the processes and devices as set forth in the prior art.

However, the article of Yang et al. does not teach S-D transformations.

The application of Weng, entitled "Methods for analysis of measurement errors in measured signals" performs second derivative transformations to analyze microarray data (see paragraphs [0064] to [0070]). The purpose of the application of Weng is described in paragraph [0010] which states:

The present invention provides methods for analyzing measurement errors in measured signals obtained in an experiment, e.g. measured intensity signals obtained in a microarray gene expression experiment or microarray proteomics experiment. Signals from any experimental measurement can be analyzed by the methods of the present invention.

It would be obvious for someone of ordinary skill in the art at the time of the instant invention to modify the microarray normalization methods of Yang et al. by use of the microarray signal transformations of Weng because while Yang et al. transforms



and plots the experimental data according to the theories proposed, Weng has the advantage of using the required S-D (second derivative) transformation for the ability to better analyze microarray signal data.

Related transformations are plotted in the Figures 1-4 of Weng (the additional limitation of instant claim 2 is a plot of the S-D transformation).

It would be obvious for someone of ordinary skill in the art at the time of the instant invention to modify the microarray normalization methods of Yang et al. by use of the microarray signal transformations of Weng because while Yang et al. transforms and plots the experimental data according to the theories proposed, Weng has the advantage of using the required S-D (second derivative) transformation for the ability to better plot error in microarray signal data.

Instant claim 13 is drawn to a species of instant claim 1 with several intermediate outputting steps after each transformation.

It would have been obvious to someone of ordinary skill in the art to repetitively output results of each intermediate transformation because it is obvious to repeat the steps of a claim. In this instance, instant claim 1 outputs results as a final step. It is obvious to repeat this step of outputting the results at various points in the claim because there is no mandating of the order in which to carry out the steps of instant claim 1. In other words, instant claim 1 can be repeated multiple times with the outputting steps at each of the same locations of the outputting steps in instant claim 13 and make obvious instant claim 13 over the prior art used for instant claim 1.

Related transformations are plotted in the Figures 1-4 of Weng (the additional limitation of instant claim 14 is a plot of the S-D transformation).

It would be obvious for someone of ordinary skill in the art at the time of the instant invention to modify the microarray normalization methods of Yang et al. by use of the microarray signal transformations of Weng because while Yang et al. transforms and plots the experimental data according to the theories proposed, Weng has the advantage of using the required S-D (second derivative) transformation for the ability to better plot microarray signal data error.

Instant claim 27 is drawn to the same method steps as instant claim 13 with the additional limitations of claims 27 having preambles indicating the method is a DNA microarray data correction program, and a computer readable medium containing the DNA microarray data correction program, respectively.

Weng discloses a computer with computer readable media in Figure 14.

It would be obvious to someone of ordinary skill in the art at the time of the instant invention to modify Yang et al. in view of the automated method of Weng because Weng can carry out the method expeditiously and accurately on a computer system.

### ***Response to Arguments***

Applicant's arguments filed 04/02/2009 have been fully considered but they are not persuasive.

In regard to the rejection of claims under 35 USC 103(a) as being unpatentable over Yang et al. in view of Weng, applicants argue various features of what the claimed process is able or intended to do.

In response, it is noted that the recited limitation have been given their full weight and consideration in light of their breadth. Although the claims are interpreted in light of the specification, limitations from the specification are not read into nor inferred in the claims. Applicant's arguments do not clearly point out the patentable novelty of the limitations recited in the claims which differentiates them from the prior art of record. Further, applicants arguments do not show how the amendments avoid such references or objections. The recent Supreme Court decision in *KSR International Co. v. Teleflex Inc.* expressly rejected the application of a rigid TSM test in determining obviousness. Applicants reiterated arguments directed toward the lack of specific teachings from the prior art that also present the identical motivations as presented by applicants disclosure are not persuasive for this reason. Further, the court ruled that "(t)he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results". In the instant case, one of ordinary skill in the art would recognize that the combination of teachings set forth by Yang et al. and Weng would yield predictable results. On this point, applicants have not identified nor presented arguments as to why the results produced by the instant claims would specifically be unexpected or unpredictable beyond that which is taught in the prior art. Therefore, the rejection of claims under 35 U.S.C. 103(a) as being unpatentable over Yang et al. in view of Weng is maintained.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. DEJONG whose telephone number is (571)272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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/ERIC S. DEJONG/

Primary Examiner, Art Unit 1631